ICD

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,645	03/19/2004	Giovanni Paternostro	GP-00102.P.1.1	7761

24232 7590 09/09/2005

DAVID R PRESTON & ASSOCIATES APC
12625 HIGH BLUFF DRIVE
SUITE 205
SAN DIEGO, CA 92130

EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/804,645	PATERNOSTRO, GIOVANNI	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 20 June 2005.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

S-20 \

DETAILED ACTION

Applicant has filed a response to the First Action on the Merits, June 20, 2005. No claims have been amended.

Claims 1-24 are under consideration.

Information Disclosure Statement

Applicant has provided a copy of document D19, Lin et al., 1998, which was cited on the IDS of December 10, 2004. The Examiner has acknowledged and considered the copy. Reference D47 has not been considered as it is a duplicate of D46.

Withdrawn Rejections

35 U.S.C. § 101-Double Patenting

Applicant's arguments, see pages 5-6 of Applicant's response, filed June 20, 2005, with respect to claims 1-10, 12-22, and 24 have been fully considered and are persuasive. The rejection of claims 1-10, 12-22, and 24 has been withdrawn. Applicant has pointed out that the inventions of Application 10/077,670 and the instant Application are not identical. The Examiner finds the argument persuasive.

35 U.S.C. § 102(b)

Applicant's arguments, see page 6-7 of Applicant's response, filed June 20, 2005, with respect to claims 17-24 have been fully considered and are

persuasive. The rejection of claims 17-24 has been withdrawn. Applicant has pointed out that Paternostro et al. (2001) do not teach that Drosophila melanogaster were subject to cardiac hypoxia or anoxia in a method of screening for effects of certain agents on cardiac function. The Examiner finds the argument persuasive.

35 U.S.C. § 103(a)

Applicant's arguments, see page 8 of Applicant's response, filed June 20, 2005, with respect to claims 1-16 have been fully considered and are persuasive. The rejection of claims 1-16 has been withdrawn. Applicant has pointed out that neither Paternostro et al (2001), Paternostro (U.S. Application 10/077,670), nor St. Johnston (2002) teach a step that includes exposing an adult Drosophila to conditions able to induce cardiac hypoxia or anoxia. The Examiner finds the argument persuasive.

New Rejections

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory

double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10 and 12-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-5, 8-19, 21-24, 31 of copending Application No. 10/077,670 ('670) in view of Haddad et al. (1997, PNAS, USA, 94: 10809-10812) and Woo et al. (1994, Ann. Rev Med. 45: 325-339). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are more narrow in scope than the claims of '670. The instant claims are drawn to an additional step of exposing the Drosophila to conditions able to induce cardiac hypoxia or anoxia.

The specification of '670 teaches that the claimed invention encompasses a method of screening for genes affecting age-associated changes in cardiac function. The specification of '670 teaches that older flies were treated with external electrical pacing (Example 6). External electrical pacing was used to estimate the maximal heart rate achievable in young and old flies. In addition to determining that older flies achieved a heart rate substantially lower than younger flies, the specification teaches that electrical pacing triggered a fibrillation-like rhythm in the hearts of flies, of which, 40% of the older flies never recover. This indicates the presence of age-associated electrophysiological defects in the hearts of aged flies. While the specification of '670 teaches monitoring Drosophila hearts in aged and young flies following external electrical pacing,

they do not teach a step of introducing the flies to conditions of anoxia and hypoxia.

Haddad et al. teach that each year, millions of individuals in the United States die or are morbidly ill because of conditions or disease that acutely reduce oxygen supply to hypoxia-sensitive tissue, such as the myocardium, central nervous system, and kidneys. While much research has been focused on the mechanism and prevention of vessel disease (e.g. atherosclerosis) that lead to stroke or myocardial infarction, little is known about the molecular mechanisms underlying the cellular responses to lack of oxygenation and how to prevent damage once a reduction in oxygen supply has occurred (Haddad et al., page 10809, 1st col., 1st parag.). Haddad et al. teach that wild type Drosophila melanogaster is extremely resistant to anoxia. This fruit fly, with an oxygen consumption rate that exceeds even mammalian levels and a total life span of several weeks, can survive hours in anoxia and apparently, not suffer tissue injury. Therefore, for Haddad, et al., the fly is a model system to study the genetic basis of anoxia tolerance. Haddad et al. teach the parameters used to induce anoxia in Drosophila (Haddad et al., page 10809, 2nd col., parag. under "Anoxia Testing").

Woo et al. teach that there are many factors that taken into account in determining what factors affect survival of a patient following a heart attack. Patients that survive acute myocardial infarction are susceptible to heart failure, recurrence of angina, reinfarction, arrhythmias, and sudden cardiac death. Aside from being susceptible to these heart conditions, prognostic factors play a role in

determining survival of a heart attack patient. In addition to considering the age of the patient, another factor is whether a patient has cardiac arrhythmia (Woo et al. abstract).

Therefore, it would have been obvious for an artisan to induce a heart attack by introducing the flies to anoxic or hypoxic condition in order to obtain flies that survive the heart attack and are susceptible to heart failure, recurrence of angina, reinfarction, arrhythmias, and sudden cardiac death, such that an artisan would then use the flies in a method of screening for genes or agents that affect heart function. Alternatively, it would have been obvious for an artisan to induce a fibrillation-like rhythm in the hearts of flies, simulate a heart attack in flies by introducing them to anoxic or hypoxic conditions and use the hypoxic/anoxic flies comprising a fibrillation-like rhythm in a method for screening for genes that affect cardiac function.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-24 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Paternostro et al. (2001, Circ. Res., 88: 1053-1058, see IDS) in view of Haddad et al. (1997, PNAS, USA, 94: 10809-10812).

Paternostro et al. teach a method of monitoring heart rate in Drosophila, wherein the study taught that maximal heart rate is significantly and reproducibly reduced with aging in Drosophila and is analogous to observations in elderly humans. Paternostro et al. indicate that the findings taught in their study will lay a foundation for the eventual application of genome-wide screens for genes that accelerate or retard age-associated heart dysfunction in Drosophila (Paternostro et al., page 1053, 2nd col., 3rd parag. to page 1054, 1st col., 1st parag.). Paternostro et al. teach that flies comprising a nucleic acid sequence encoding green fluorescent protein (GFP) operably linked to the distal actin 5c promoter were used in their studies (Paternostro, et al, page 1054, 2nd col. under "Experiments with GFP Transgenic Flies"). These flies expressed GFP in their hearts. Paternostro et al. teach that their work is the first time other aspects of cardiac physiology, including an age-associated increase in rhythm disturbances, of young and aging Drosophila was monitored (Paternostro, et al., abstract). In this method, heart rate and its variation was directly recorded on a single fly by video signals. Anesthetized flies were mounted on glass slides and were observed on an inverted microscope with Nomarski optics (Paternostro et al., page 1054, 1st col. under "Measurements of Heart Rates"). Images of flies were obtained by closing the diaphragm so that the light beam was concentrated on the first ventricle of the heart (Paternostro et al., page 1054, 1st col. under

"Measurements of Heart Rates"). In the case of visualizing heartbeats of GFP flies, Paternostro et al. teach two fluorescent microscopes were used. One was the Heidelberg Retina Angiograph, a confocal laser-scanning system developed for digital fluorescein angiography in ophthalmic patients. The other was a Bio-Rad MRC-1024 confocal microscope (Paternostro et al., page 1054, parag. under "Experiments with GFP Transgenic Flies"). Flies were positioned on their backs, perpendicular to the light path and fixed in this position on a glass slide with double-stick tape. Images were of the first ventricle of the heart, which were recorded by using a Sony DXC-101 videocamera on VHS tape. End-diastolic and end-systolic dimensions were measured on still images at the midpoint between the 2 major transversal tracheal tubes passing over the first cardiac ventricle (Paternostro et al., page 1054, 1st col. under "Measurements of Heart Rates" and 2nd col. under "Automated Heart Rate Detection"). Paternostro et al. teach that the average heart rate decreased progressively with age. While flies at 10 days of age had a mean heart rate of 286 beats per minute (bpm), flies at 31 days of age has 249 bpm and flies at 54 days of age had 220 bpm (Paternostro et al., page 1055, 1st col. under "Resting Heart Rate Declines with Age in Drosophila"). Paternostro et al. also teach that temperature stress had a more pronounced effect of age on average heart rate. For every age group examined, increased ambient temperature resulted in a faster heart rate (Paternostro et al., page 1055, parag. under "Temperature Stress Tests Reveal Age-Associated Cardiac Impairment in Drosophila"). In addition to these studies, Paternostro et al. teach that heart rate variability between young and aged flies

was different. The coefficient of variation of heart rate was significantly larger in older flies (14.8+/-1.4) versus 9.2+/-0.4 in young flies. These values were obtained from heart wall displacement plots obtained with automated heart rate detection software (Paternostro et al., page 1056, parag. under "Heart Rate Variability" and Figure 5).

While Paternostro et al. teach a method of monitoring heart rate and rhythm disturbances in young and aging Drosophila, they do not teach a method of initially treating adult Drosophila to anoxic or hypoxic conditions before or during a screen for a gene or an agent affecting cardiac function.

Haddad et al. teach that each year, millions of individuals in the United States die or are morbidly ill because of conditions or disease that acutely reduce oxygen supply to hypoxia-sensitive tissue, such as the myocardium, central nervous system, and kidneys. While much research has been focused on the mechanism and prevention of vessel disease (e.g. atherosclerosis) that lead to stroke or myocardial infarction, little is known about the molecular mechanisms underlying the cellular responses to lack of oxygenation and how to prevent damage once a reduction in oxygen supply has occurred (Haddad et al., page 10809, 1st col., 1st parag.). Haddad et al. teach that wild type Drosophila melanogaster is extremely resistant to anoxia. This fruit fly, with an oxygen consumption rate that exceeds even mammalian levels and a total life span of several weeks, can survive hours in anoxia and apparently, not suffer tissue injury. Therefore, for Haddad, et al., the fly is a model system to study the genetic basis of anoxia tolerance. Haddad et al. teach the parameters used to

induce anoxia in Drosophila (Haddad et al., page 10809, 2nd col., parag. under "Anoxia Testing").

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use adult Drosophila in a method for screening for genes or agents that affect cardiac function during or after hypoxia or anoxia, wherein the method for screening comprises exposing adult Drosophila to conditions able to induce cardiac hypoxia or anoxia, imaging the heart of said Drosophila, measuring the movements of the heart in the image, analyzing the measurements of the movements, and identifying a gene or agent affecting the cardiac function of Drosophila.

One having ordinary skill in the art would have been motivated to include a step of inducing cardiac hypoxia or anoxia in Drosophila to the method taught by Paternostro et al. Motivation was provided by Haddad et al. teaching that one of the tissues affected by anoxic/hypoxic insult is myocardium and that Drosophila was an ideal model system to study what genes are implicated in prevention of tissue injury in flies following anoxic/hypoxic insult. Motivation was also provided by Paternostro et al teaching that their study will lay a foundation for the eventual application of genome-wide screens for genes that accelerate or retard age-associated heart dysfunction. The method taught by Paternostero et al. would be ideal for monitoring arrhythmia in Drosophila following anoxic/hypoxic insult, such that an artisan can identify genes or agents which can be used to reduce tissue damage in the myocardium of flies and reduce the events that lead up to cardiac death.

There would have been a reasonable expectation of success given the results of Paternostro et al. for teaching the method of screening for agents that affect heart rhythm in flies, for Haddad et al. for teaching that Drosophila melanogaster is an ideal organism which can be used to model a human condition.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When

calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER